Effects of exogenous insulin on glucose tolerance in alpacas

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Objective—To evaluate the effects of exogenous insulin on clearance of exogenous glucose in alpacas.

Animals—7 adult castrated male alpacas.

Procedure—Prior to each of 2 trials, food was withheld for 8 hours. Glucose (0.5 g/kg of body weight) was then administered by rapid IV infusion. During 1 of the trials, regular insulin (0.2 U/kg, IV) was also administered 15 minutes later. Blood was collected immediately before (0 minutes) and 15, 20, 25, 30, 45, 60, 90, 120, 180, and 240 minutes after glucose administration. Plasma concentrations of glucose and lactate were determined, and glucose fractional turnover rate and plasma half-life were calculated.

Results—Insulin treatment caused a significant increase in fractional turnover rate of glucose and plasma lactate concentration. Plasma glucose concentrations were lower in insulin-treated alpacas from 30 minutes after glucose administration (15 minutes after insulin administration) until the conclusion of each trial, compared with nontreated alpacas. In addition, plasma glucose concentration in insulin-treated alpacas returned to baseline values 1 hour sooner than in the nontreated group.

Conclusions and Clinical Relevance—Glucose uptake in alpacas improves after insulin treatment, suggesting that administration of exogenous insulin will increase the therapeutic and decrease the pathologic effects of exogenous glucose administered to hypoglycemic alpacas. However, alpacas and other New World camelids should be monitored carefully during treatment with glucose or insulin, because these species appear to be partially insulin resistant. (Am J Vet Res 2001;62:1544–1547)

Insulin is used to treat many disorders of energy metabolism in domestic animals, including diabetes mellitus, ketosis, and hepatic lipidosis. It has also been used, without proof of efficacy, to treat possible diabetes mellitus, hepatic lipidosis, hyperosmolar disorder, and other hyperglycemic or hyperlipemic conditions in llamas and alpacas. Similarly, glucose is often administered to anorectic or hypoglycemic camelids according to protocols developed to supply energy to other species. However, blood insulin concentrations are less and clearance rates of exogenous glucose are slower in llamas and alpacas, compared with other domestic ruminants.

Materials and Methods

Alpacas—Seven adult castrated male alpacas were used. All had been maintained on pasture and supplemented with orchard grass hay for several months. Alpacas were acclimated to stalls and handling areas for 96 hours before the study and judged to be healthy on the basis of history and results of physical examination, CBC, and serum biochemical analyses. A 16-gauge double-lumen IV catheter was placed into the right jugular vein of each alpaca 2 days before the study. Before and between trials, alpacas were housed in groups to minimize stress.

Experimental design—This study was conducted with approval of the Institutional Animal Care and Use Committee of Oregon State University. For each alpaca, 2 trials were performed on subsequent days. The order in which the trials were performed was determined randomly. Before each trial, food was withheld for 8 hours. A time-0 blood sample was collected into tubes containing sodium fluoride and immediately thereafter, alpacas received a 50% glucose solution (0.5 g/kg of body weight) by rapid (< 10 seconds) injection through 1 lumen of the IV catheter. Subsequent
blood samples (15, 20, 25, 30, 45, 60, 90, 120, 180, and 240 minutes after glucose injection) were collected through the other lumen of the catheter after discarding the first 5 ml of blood withdrawn. In 1 of the 2 trials, regular insulin (0.2 U/kg) was also administered IV immediately following collection of the 15-minute blood sample. After both trials were completed, the jugular catheters were removed, and alpacas were fed and returned to the herd.

Determination of plasma glucose and lactate concentrations—Blood samples were placed on ice, and fluoridated plasma was separated from erythrocytes within 20 minutes of collection. Samples were analyzed for glucose and lactate concentration by use of an automated chemistry analyzer.1

Determination of glucose and kinetics—The fractional turnover rate of glucose (glucose disappearance rate; k) was calculated for each interval after insulin administration, using the formula:

\[
k (\text{%/min}) = \frac{\ln[\text{glucose}]_1 - \ln[\text{glucose}]_2}{\text{interval}_{\text{min}}} \times 100
\]

Fractional turnover rate and plasma half-life \((T_{1/2})\) of glucose were also calculated for the period from 15 to 45 minutes after glucose infusion. Plasma half-life was determined by use of the formula:

\[T_{1/2} (\text{min}) = \frac{0.693}{k} \times 100\]

Statistical analyses—Data were expressed as mean ± SD. Effects of time and insulin on plasma concentrations of glucose and lactate were analyzed by use of 2-way ANOVA for repeated measures.2 Differences between mean values were assessed by use of the Tukey test. Fractional turnover rates for each interval were also compared between insulin-treated and untreated alpacas by use of a 2-way ANOVA for repeated measures and the Tukey test. Fractional turnover rate and \(T_{1/2}\) of glucose determined for the period from 15 to 45 minutes after glucose infusion were compared between insulin-treated and untreated alpacas by use of a paired \(t\)-test. For all tests, differences were considered significant at \(P < 0.05\).

Results

Glucose concentration—Mean plasma glucose concentrations differed significantly \((P = 0.013)\) between trials. In addition, the interaction of treatment and time significantly \((P < 0.001)\) affected glucose concentration. Glucose concentrations at 0 (preinfusion) or 15 (postglucose, preinsulin) minutes did not differ between trials. However, beginning 15 minutes after insulin injection (30-minute sample) until completion of the trial, mean glucose concentrations in alpacas treated with glucose and insulin were less than in alpacas treated with glucose alone (Fig 1). Glucose concentrations in alpacas treated with insulin returned to preinfusion values within 3 hours, whereas concentrations in alpacas treated with glucose alone returned to preinfusion values within 4 hours.

Glucose kinetics—A significant \((P = 0.010)\) difference in fractional turnover rate of glucose was detected between treatment trials. Again, the interaction of treatment and time significantly \((P < 0.001)\) affected turnover rate. In alpacas treated with glucose and insulin, mean fractional turnover rates were significantly higher for the first 5 intervals or 45 minutes, compared with alpacas treated with glucose alone (Fig 2). Mean fractional turnover rate peaked at 1.38 ±
provided an indirect measure of cellular glucose uptake. In many species, glucose tolerance testing leads to an increase in lactate production, because excess intracellular glucose is incompletely oxidized to lactate by extrahepatic tissues. This increase does not occur during glucose tolerance testing in healthy llamas and alpacas, suggesting that extrahepatic tissues in these animals assimilate exogenous glucose poorly. On the basis of results of the present study, poor glucose assimilation (measured as low glucose clearance and high lactate concentrations) can be overcome to some degree by the administration of exogenous insulin. However, as judged by the peak lactate concentration, exogenous glucose assimilation was less in insulin-treated alpacas than in untreated members of other species.

Even though alpacas have low concentrations of endogenous insulin, fractional turnover rates of glucose are less and clearance half-times of glucose are longer in clinically normal alpacas than in dogs with type-I or type-II diabetes mellitus. This suggests that other mechanisms of glucose clearance, such as insulin-independent cellular uptake or renal loss, are active in alpacas. Urinary glucose loss has been documented in Old World camels after IV infusion of glucose. The renal threshold for glucose excretion has not been established in alpacas. However, from our experience, it is likely to be low, and renal loss of glucose is likely to be an important mechanism by which camels avoid chronic hyperglycemia.

Our data suggest that although the response was weak, insulin may be administered in conjunction with glucose to improve glucose assimilation and avoid pathologic changes in osmolality. However, more research is necessary to determine the correct protocols for insulin and glucose administration in alpacas. In addition, it cannot be ascertained from our results whether insulin can be used to treat naturally occurring hyperglycemia. The action of regular insulin lasted for 45 minutes and enabled a more rapid return to baseline plasma glucose concentrations. Administration of higher insulin doses would be unlikely to improve glucose uptake to a greater degree, because the dose we used was the same used to treat hyperglycemia in other species. This dose should have resulted in blood insulin concentrations far in excess of those necessary to saturate receptors. Administration of longer acting forms, repeated doses, or slow infusions of insulin may allow for greater glucose assimilation but may also induce hypoglycemia in camels that do not receive exogenous glucose. Therefore, careful monitoring of plasma glucose concentrations during and after glucose or insulin administration in camels is recommended to avoid pathologic changes in blood glucose concentrations or osmolality.

References

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